REMARKS/ARGUMENT

The withdrawal of claims 8-11 is noted. It is respectfully that in view of the comments below, there will be an allowable generic or linking claim and these claims should also be examined.

An obvious correction in claim 12 has been made. In addition, the dependency of this claim has been changed so that it is not a substantial duplicate of claim 4.

Claims 1-5, 7, 12, 13 and 16-18 have been rejected under 35 USC 103 over the newly cited Schafer patent in view of Tosa. This rejection is respectfully traversed.

The present invention is concerned with a kinetic assay during the course of which a component of the system becomes at least partially bound, directly or indirectly, to the surface of a solid body. The Applicants recognized that during the course of such an assay, a reliable measurement of the bound or absorbed component, i.e., without interference from the free component in the assay system, can be obtained by direct continuous monitoring of the component. This allows an indication of the unknown ligand concentration to be obtained at a very early stage of the incubation period without the need to wait for an arbitrarily determined end point, such as the equilibrium steady state condition. As a result, the operator can observe the result continuously and judge whether it is worthwhile taking further readings in an attempt to improve the accuracy of the results. This continuous monitoring also allows random errors caused by problems with instrumentation, for instance, to be readily identified.

Claim 1 recites the three steps involved in the invention. First, an analyte dependent parameter (such as, for example, a fluorescent emission) is measured kinetically in a direct and continuous manner from a time after the onset of incubation. In the second step, the measured kinetic data is manipulated to quantitatively determine the unknown sample and in the third step, the results of the determination are monitored continuously. There is no teaching or suggestion of this method in the cited references.

Kinetic measurements have been used in certain prior art immunosensors. Here, the rate of change of signal of the sample containing an unknown quantity of antigen is measured and compared with the same parameter for standards containing a known concentration of the antigen. That technique suffers from the drawback that the assay must be allowed to obtain an

arbitrary determined equilibrium at which point a single end point measurement of the signal is made. The speed with which equilibrium is reached may be prohibitively slow, and this, in itself, can introduce errors in the measured rate of change of signal which will be critically dependent on the prevailing conditions. It is not possible in such a system to obtain quick and accurate measurements of the ligand concentration.

The Schäfer reference is an improvement in the known kind of immunoassays. The improvement in Schäfer resides in how to manage those assays, in which the calibration curve $X=f^{1}(C)$ (where C is the concentration and X is a variable derivable from the measurement of a parameter S which varies during the assay) does not have a monotonous shape (column 6, lines 4-14 and 40-42). Schäfer provides a way to reduce the errors and variables linked to these types of assays which were known at the time of that reference. This is done by using operative discriminative algorithms, as noted in column 4, lines 4-43. The deficiencies in the known kinetic assays are therefore equally applicable to Schäfer.

The Office Action acknowledges that Schäfer differs from the claimed invention in that it performs the immunoreactions in solution rather than a solid surface. That difference is important because in the assay claimed, the component which is directly and continuously measured becomes bound to a solid body and therefore what is being measured during the assay is only this bound component. That avoids interference with any free component in the solution, thereby providing the advantages described in the present application.

The Office Action relies on the Tosa reference as disclosing an assay involving an immunochemical binding reaction on a waveguide surface in order to enable the monitoring of a reaction by luminescence detection. Applicants have previously discussed Tosa in detail in, e.g., the April 2000 Amendment, and incorporate that discussion herein by reference.

The Office Action alleges that it would be obvious to substitute the heterogeneous method of Tosa for the homogeneous method of Schäfer on the grounds that it is an art recognized equivalent method for detecting a binding reaction as well as providing the capability of fast detection response and simplified detector design. In response, applicants respectfully submit that this is a hindsight justification of the proposed combination and there is no motivation or justification for the combination in the absence of hindsight. Tosa provides no suggestion of a continuous monitoring of results of the determination nor of any possible advantage in carrying out any kinetic measurement. The two references refer to two different

kinds of assays and are designed to solve different problems. Schäfer 's assay is intended to provide an improved method of assay to overcome the problems of ambiguity associated with homogenous methods of analysis in which the calibration curve does not have a monotonous shape (column 1, line 51 to column 2, line 15 and column 3, lines 60-65). The solution is provided by using a discrimination algorithm (column 3, line 66 to column 4, line 43). Tosa, in contrast, is concerned with providing a new optical waveguide (i.e. heterogeneous) based method for measuring the degree of immunity reaction, which does not involve or suggest a continuous monitoring of results of the determination.

Applicants respectfully submit that the persons skilled in the art would not be motivated to modify the already improved method of Schäfer in any further way. Even in the unlikely event that there was such motivation, then the artisan would not combine the teachings of Schäfer with Tosa as the latter reference relates to a different type of assay and is directed to solving a different type of problem.

Beyond the foregoing, it is respectfully pointed out that Schäfer solves the problems posed by the prior art assays in a completely different matter, i.e. by using operatively discrimination of algorithms, which are determined during the calibration step and that are reported to reduce errors in the measurement results. No such algorithm is necessary according to the present invention because the component becomes bound to the solid surface and can, surprisingly, be measured directly and continuously without interference from the free component in solution. That already reduces errors and variables in the assay. The present invention represents an alternative, more simple solution to the problem solved by Schäfer, and is not taught or suggested in either Schäfer or Tosa, whether considered alone or in combination.

In light of all of these considerations, it is respectfully submitted that the obviousness rejection should be withdrawn.

Claims 6 and 14 were rejected under 35 USC 103 over Schäfer in view of Tosa in further view of Sutherland. Given the fact that the claims on which these claims are dependent are patentable over the combination of Schäfer and Tosa, it is respectfully submitted that these claims are also patentable. Sutherland does not cure any of the deficiencies in that prior rejection. Sutherland relates to the use of an optical waveguide for optically ascertained parameters of the species and a liquid analyte. It, like Tosa, always uses steady state

measurements to establish a relationship between those values. It is therefore respectfully submitted that this rejection should also be withdrawn.

In light of all of the foregoing considerations, it is respectfully submitted that this application is now in condition to be allowed and the early issuance of a Notice of Allowance is respectfully requested.

Respectfully submitted,

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APPENDIX A
Version With Markings To Show Changes Made
37 C.F.R. § 1.121(b)(1)(iii) AND (c)(1)(ii)

CLAIMS:

12. A method as claimed in claim [1] 2 wherein said [analyte parameter] kinetic data is fluorescence emission.